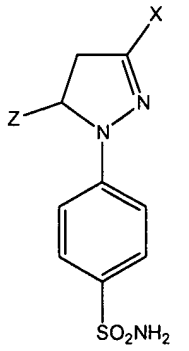
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Amended) A compound of the formula I:



(I)

wherein:

X is [selected from the group consisting of] trihalomethyl [and C_1-C_6 alkyl]; and

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof.

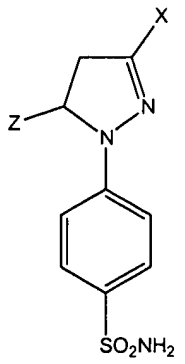
2. (Original) A compound according to claim 1 wherein Z is selected from the group consisting of substituted and unsubstituted heteroaryl; or a pharmaceutically acceptable salt thereof.

3. (Twice amended) A compound according to claim 2 wherein [[Z]] said heteroaryl is selected from the group consisting of [substituted and unsubstituted] indolyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, imidazolyl, pyrazolyl, thiazolyl, [benzothazolyl] benzothiazolyl, quinolinyl, and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

4. (Original) A compound according to claim 1 wherein Z is 3-indolyl; or a pharmaceutically acceptable salt thereof.

5. (Original) A compound according to claim 1 wherein X is trifluoromethyl.

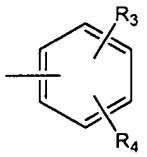
6. (Twice amended) A compound of the formula I:



(I)

wherein:

X is a group of formula II:



(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted heteroaryl; phenyl which is mono-substituted with hydroxyl, nitro, carboxy, C_1-C_6 trihaloalkyl or cyano; phenyl which is di-substituted; and phenyl which is tri-substituted; [aryl, and]

provided when Z is substituted or unsubstituted heteroaryl, it is selected from the group consisting of [substituted and unsubstituted] pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl);

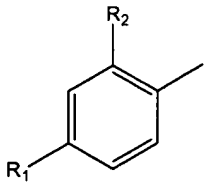
or a pharmaceutically acceptable salt thereof.

7. (Twice amended) A compound according to claim 6 wherein Z is selected from the group consisting of [unsubstituted phenyl; and] phenyl mono-substituted with

hydroxyl, nitro, carboxy, C_1-C_6 trihaloalkyl or cyano, [[di-]] di-substituted phenyl and tri-substituted phenyl.

8. (Amended) A compound according to claim 7 wherein Z is phenyl substituted with one or more of [halogen,] hydroxyl, nitro, [C_1-C_6 alkyl, C_1-C_6 alkoxy,] or carboxy; or a pharmaceutically acceptable salt thereof.

9. (Amended) A compound according to claim [10] 6 wherein Z is the group:



(III)

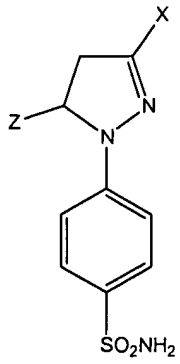
wherein R_1 and R_2 are independently selected from the group consisting of [hydrogen,] fluorine, bromine, chlorine, C_1-C_3 alkyl, C_1-C_3 alkoxy, hydroxyl and nitro; or a pharmaceutically acceptable salt thereof.

10. (Amended) A compound according to claim 6 wherein Z is substituted or unsubstituted heteroaryl, wherein said heteroaryl is indolyl, furyl, pyridyl or benzofuryl; or a pharmaceutically acceptable salt thereof.

11. (Original) A compound according to claim 10 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

12. (Original) The compound according to claim 1 which is 1-(4-sulfamylphenyl)-3-trifluoromethyl-5-(3-indolyl)-2-pyrazoline; or a pharmaceutically acceptable salt thereof.

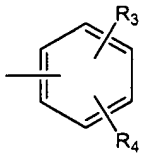
13. (Amended) A compound of the formula I:



(I)

wherein:

X is a group of formula II:



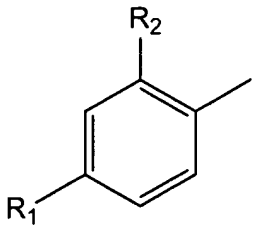
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and C_1-C_6 alkoxy;

Z is selected from the group consisting of [phenyl;] phenyl monosubstituted with [halogen,] hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and substituted and unsubstituted heteroaryl, wherein said heteroaryl is selected from the group consisting of [substituted and unsubstituted] pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

14. (Amended) A compound according to claim 13 wherein Z is the group:



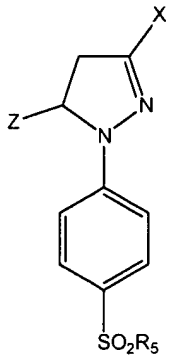
(III)

wherein R_1 and R_2 are independently selected from the group consisting of fluorine, bromine, chlorine, C_1-C_3 alkyl, C_1-C_3 alkoxy, hydroxyl and nitro; or a pharmaceutically acceptable salt thereof.

15. (Amended) A compound according to claim 13 wherein Z is substituted or unsubstituted heteroaryl, wherein said heteroaryl is indolyl, furyl, pyridyl or benzofuryl; or a pharmaceutically acceptable salt thereof.

16. (Original) A compound according to claim 15 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

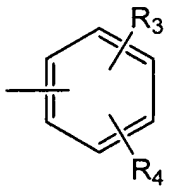
17. (Amended) A compound of the formula V:



(V)

wherein:

X is selected from the group consisting of trihalomethyl, C_1-C_6 alkyl, and a group of formula II:



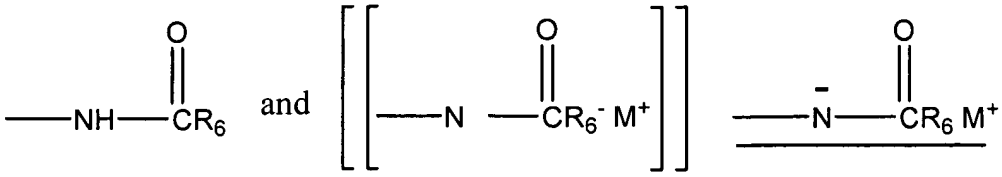
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano;

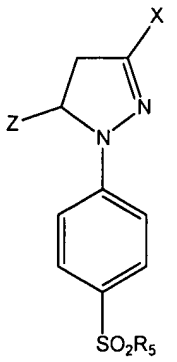
Z is substituted or unsubstituted heteroaryl; and

R_5 is selected from the group consisting of:



wherein R_6 is C_1-C_6 alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof.

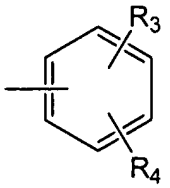
18. (Amended) A compound of the formula V:



(V)

wherein:

X is a group of formula II:



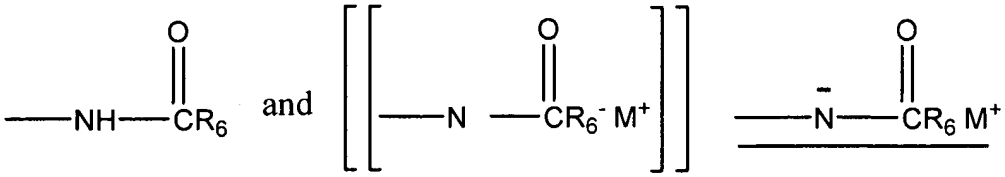
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6, alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl; and

R_5 is selected from the group consisting of:



wherein R_6 is C_1-C_6 alkyl and M is Na, K or Li or a pharmaceutically acceptable salt thereof.

19. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

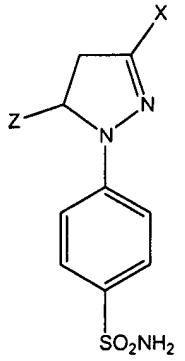
20. (Twice Amended) A method for treating a cyclooxygenase-2-mediated disorder comprising administering to a patient in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof, wherein said disorder is selected from the group consisting of colon cancer, breast cancer, brain cancer, prostate cancer, pancreatic cancer, lung cancer, and bladder cancer.

21. (Twice Amended) A method for treating inflammation [or an inflammation-mediated disorder], wherein said inflammation is mediated by cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

22. (Canceled)

23. (Canceled)

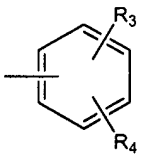
24. (Twice amended) A method for producing a compound of formula I:



(I)

wherein:

the group X is [selected from the group consisting of] trihalomethyl[, C_1-C_6 alkyl, and a radical of formula II:



(II)

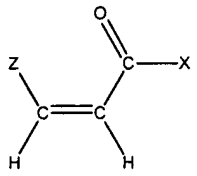
wherein:

wherein R_3 and R_4 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, nitro, C_1-C_6 alkyl, C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano]; and

Z is selected from the group consisting of substituted and unsubstituted aryl, other than substituted and unsubstituted phenyl;

the method comprising:

(a) reacting a compound of the formula IV:



(IV)

wherein X and Z are so defined;

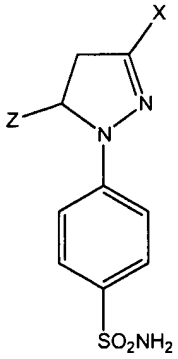
with 4-sulfamyl phenyl hydrazine or a salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

25. (Original) A method according to claim 24 wherein Z is substituted or unsubstituted heteroaryl.

26. (Canceled)

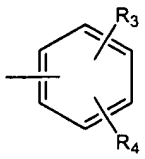
27. (Twice amended) A method for producing a compound of formula I:



(I)

wherein:

the group X is a radical of formula II:



(II)

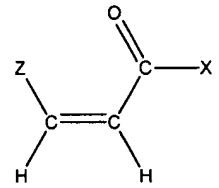
wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, nitro, C_1-C_6 alkyl, C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is selected from the group consisting of substituted and unsubstituted [aryl] heteroaryl; phenyl which is mono-substituted with hydroxyl, nitro, carboxy; C_1-C_6 trihaloalkyl or cyano; phenyl which is di-substituted, and phenyl which is tri-substituted;

the method comprising:

(a) reacting a compound of the formula IV:



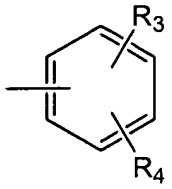
(IV)

wherein X and Z are so defined;

with 4-sulfamyl phenyl hydrazine or salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

28. (Amended) A method according to claim 27 wherein the group X in the reactant compound of formula IV is a radical of formula II:



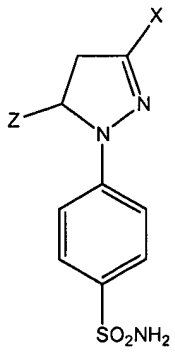
(II)

wherein:

[wherein] R_3 and R_4 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, nitro, C_1-C_6 alkyl, C_1-C_6 alkoxy; and carboxy.

29. (Original) An isolated optical isomer of a compound according to claim 17 or 18, or a pharmaceutically acceptable salt thereof.

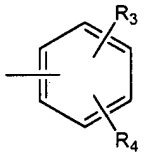
30. (Amended) An isolated optical isomer of a compound of the formula I:



(I)

wherein:

X is [selected from the group consisting of trihalomethyl, C_1-C_6 alkyl, and] a group of formula II:



(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl;

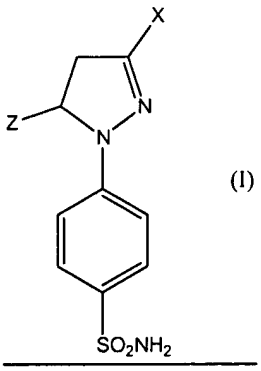
or a pharmaceutically acceptable salt thereof.

31. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 1.

32. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 6.

33. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 13.

34. (Thrice amended) A method for treating a cyclooxygenase-2-mediated disorder comprising administering to a patient in need of such treatment an effective amount of a compound according to [claim 1] formula I:



(I)

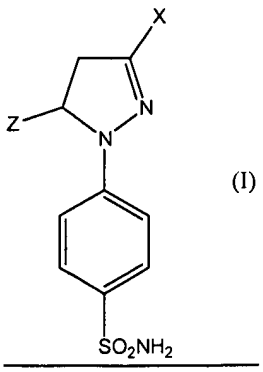
wherein:

X is selected from the group consisting of trihalomethyl and C_1-C_6 alkyl;

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof,

further wherein said disorder is selected from the group consisting of colon cancer, breast cancer, brain cancer, prostate cancer, pancreatic cancer, lung cancer, and bladder cancer.

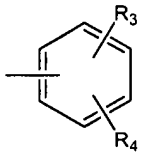
35. (Four times amended) A method for treating a cyclooxygenase-2-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 6] formula I:



(I)

wherein:

X is a group of formula II:



(II)

wherein:

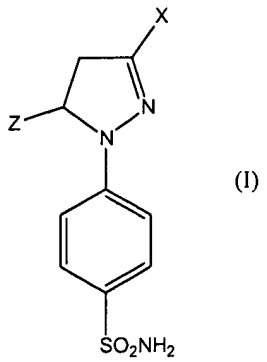
R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl, and substituted and unsubstituted heteroaryl;

wherein said heteroaryl is selected from the group consisting of pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof,

further wherein said disorder is selected from the group consisting of colon cancer, breast cancer, brain cancer, prostate cancer, pancreatic cancer, lung cancer, and bladder cancer.

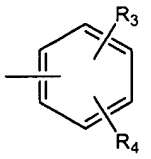
36. (Four times Amended) A method for treating a cyclooxygenase-2-mediated disorder comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 13] formula I:



(I)

wherein:

X is a group of formula II:



(II)

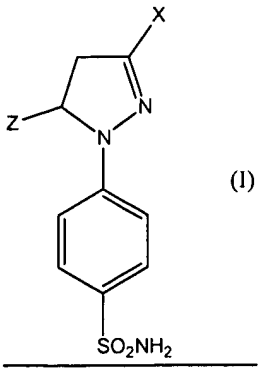
wherein:

R_3 and R_4 are independently selected from the group consisting of C_1-C_6 alkyl and C_1-C_6 alkoxy;

Z is selected from the group consisting of phenyl; phenyl monosubstituted with halogen, hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and substituted and unsubstituted heteroaryl, wherein said heteroaryl is selected from the group consisting of pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof,

further wherein said disorder is selected from the group consisting of colon cancer, breast cancer, brain cancer, prostate cancer, pancreatic cancer, lung cancer, and bladder cancer.

37. (Thrice amended) A method for treating inflammation [or an inflammation-mediated disorder], wherein said inflammation is mediated by cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 1] formula I:



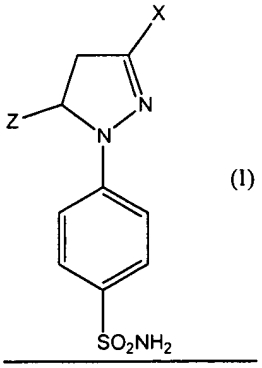
(I)

wherein:

X is selected from the group consisting of trihalomethyl and C_1-C_6 alkyl;

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl; or a pharmaceutically acceptable salt thereof.

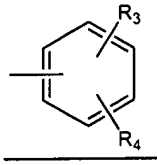
38. (Thrice amended) A method for treating inflammation [or an inflammation-mediated disorder], wherein said inflammation is mediated by cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 6] formula I:



(I)

wherein:

X is a group of formula II:



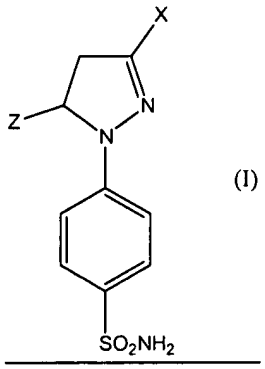
(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; carboxy; C_1-C_6 trihaloalkyl; and cyano;

Z is selected from the group consisting of substituted and unsubstituted aryl, and when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted pyridyl, furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

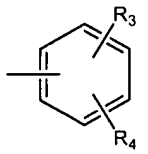
39. (Thrice amended) A method for treating inflammation [or an inflammation-mediated disorder], wherein said inflammation is mediated by cyclooxygenase-2, comprising administering to a subject in need of such treatment an effective amount of a compound according to [claim 13] formula I:



(I)

wherein:

X is a group of formula II:



(II)

wherein:

R_3 and R_4 are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl and C_1-C_6 alkoxy;

Z is selected from the group consisting of phenyl; phenyl monosubstituted with halogen, hydroxyl, nitro or carboxy; disubstituted phenyl; trisubstituted phenyl; and heteroaryl selected from the group consisting of substituted and unsubstituted pyridyl,

furyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

40-41. (Canceled)

42. (Original) A method according to claim 40 or 41 wherein Z is selected from the group consisting of substituted and unsubstituted heteroaryl; or a pharmaceutically acceptable salt thereof.

43. (Amended) A method according to claim 42 wherein [[Z]] said heteroaryl is selected from the group consisting of substituted and unsubstituted indolyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, imidazolyl, pyrazolyl, thiazolyl, benzothiazolyl, quinolinyl, and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

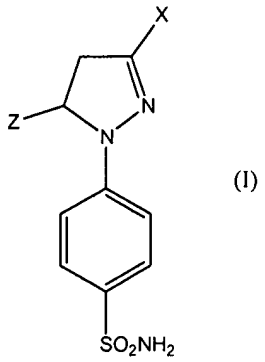
44. (Original) A method according to claim 43 wherein Z is substituted or unsubstituted 3-indolyl; or a pharmaceutically acceptable salt thereof.

45. (Original) A method according to claim 40 or 41 wherein X is trifluoromethyl.

46. (Original) A method according to claim 40 or 41 wherein X is a group according to formula II wherein R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1 -C_6 trihaloalkyl; and cyano; or a pharmaceutically acceptable salt thereof.

47. (Original) A method according to claim 46 wherein Z is selected from the group consisting of unsubstituted phenyl; and mono-, di- and tri-substituted phenyl.

48. (New) A compound of the formula I:



(I)

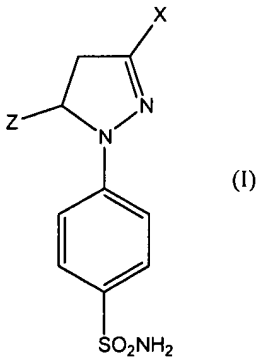
wherein:

X is C_1-C_6 alkyl; and

Z is selected from the group consisting of substituted and unsubstituted aryl other than substituted and unsubstituted phenyl;

provided when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted pyridyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl); or a pharmaceutically acceptable salt thereof.

49. (New) A method for producing a compound of formula I:



(I)

wherein:

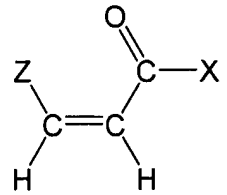
the group X is C_1-C_6 alkyl; and

Z is selected from the group consisting of substituted and unsubstituted aryl, other than substituted and unsubstituted phenyl;

provided when Z is heteroaryl, it is selected from the group consisting of substituted and unsubstituted pyridyl, indolyl, benzothienyl, benzofuryl, imidazolyl, pyrazolyl, 2-thiazolyl, quinolinyl and 4-(2-benzyloxazolyl);

the method comprising:

(a) reacting a compound of the formula IV:



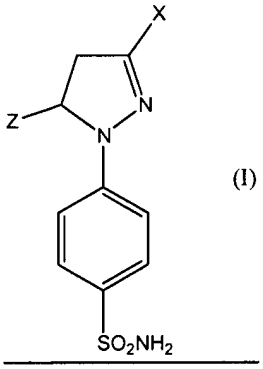
(IV)

wherein X and Z are so defined;

with 4-sulfamyl phenyl hydrazine or a salt thereof; and

(b) isolating a compound according to formula I from the reaction products.

50. (New) An isolated optical isomer of a compound of the formula I:



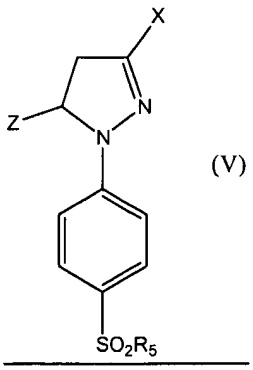
(I)

wherein:

X is selected from the group consisting of trihalomethyl and C_1-C_6 alkyl;

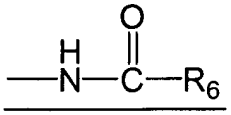
Z is selected from the group consisting of substituted and unsubstituted heteroaryl; phenyl that is mono-substituted or di-substituted with substituents independently selected from the group consisting of hydroxyl, nitro, and carboxy; and phenyl that is tri-substituted; or a pharmaceutically acceptable salt thereof.

51. (New) A method for producing a compound of formula V:



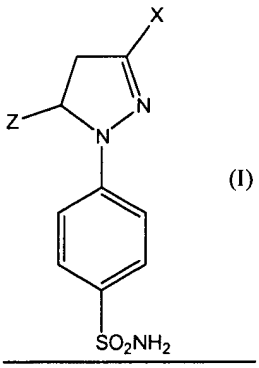
(V)

wherein R_5 is:



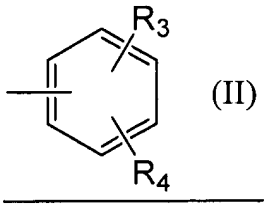
wherein R_6 is C_1-C_6 alkyl; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



(I)

wherein X is selected from the group consisting of trihalomethyl, C_1-C_6 alkyl and a group of the formula II:



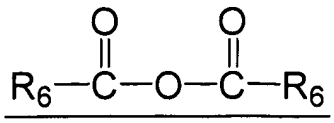
(II)

wherein:

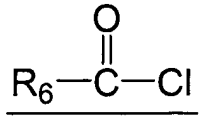
R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is substituted or unsubstituted heteroaryl;

with an anhydride of the formula:



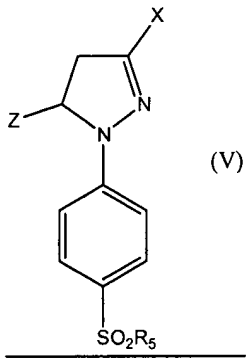
or an acylating compound of the formula:



wherein R_6 is C_1-C_6 alkyl; and

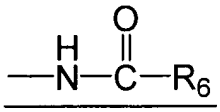
(b) isolating a compound according to formula V from the reaction products.

52. (New) A method for producing a compound of formula V:



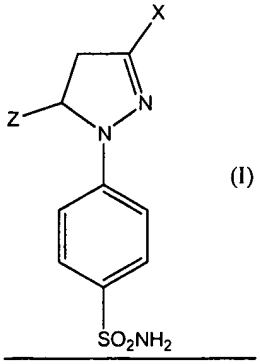
(V)

wherein R_5 is:



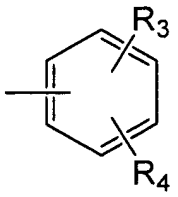
wherein R_6 is C_1-C_6 alkyl; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



(I)

wherein X is a group of the formula II:

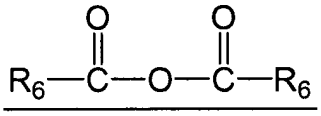


(II)

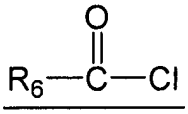
wherein: R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is substituted or unsubstituted aryl;

with an anhydride of the formula:



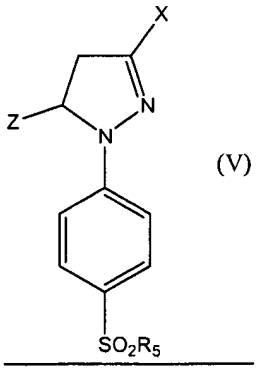
or an acylating compound of the formula:



wherein R_6 is C_1-C_6 alkyl; and

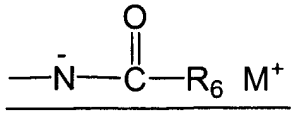
(b) isolating a compound according to formula V from the reaction products.

53. (New) A method for producing a compound of formula V:



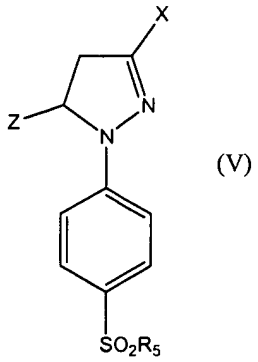
(V)

wherein R_5 is:



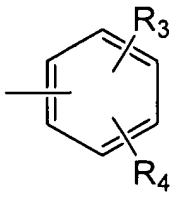
wherein R_6 is C_1-C_6 alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



(V)

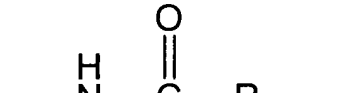
wherein X is selected from the group consisting of trihalomethyl, C_1-C_6 alkyl and a group of the formula II:



(II)

wherein: R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is substituted or unsubstituted heteroaryl; and

R_5 is 

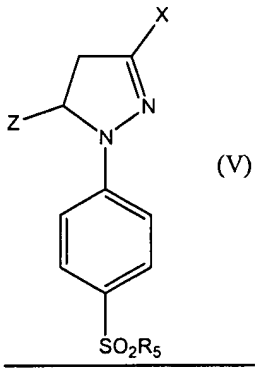
; and

wherein R_6 is as defined above,

with an alkali hydroxide selected from the group consisting of NaOH, KOH and LiOH; and

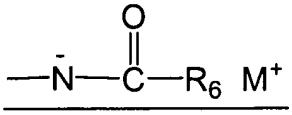
(b) isolating a compound according to formula V from the reaction products.

54. (New) A method for producing a compound of formula V:



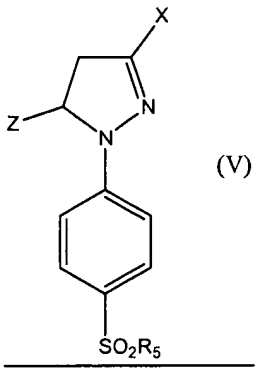
(V)

wherein R_5 is:



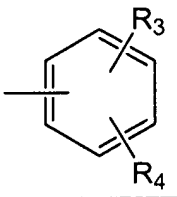
wherein R_6 is C_1-C_6 alkyl and M is Na, K or Li; or a pharmaceutically acceptable salt thereof; the method comprising:

(a) reacting a compound of formula I:



(V)

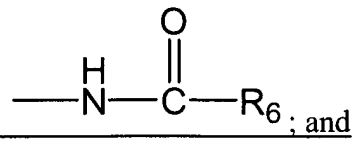
wherein X is a group of the formula II:



(II)

wherein: R_3 and R_4 are independently selected from the group consisting of hydrogen; halogen; hydroxyl; nitro; C_1-C_6 alkyl; C_1-C_6 alkoxy; carboxy; C_1-C_6 trihaloalkyl; and cyano; and

Z is substituted or unsubstituted aryl; and

R_5 is  ; and

wherein R_6 is as defined above,

with an alkali hydroxide selected from the group consisting of NaOH, KOH and LiOH; and

(b) isolating a compound according to formula V from the reaction products.